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Reviewer Comments

The authors attempt to discuss the factors that led to good or bad prognosis in neonates with hyperammonemia.

This is a retrospective study which introduces biases when there are already many variables, but understand in rare diseases, this is all we have.

Reply: Thank you for the summarizing.

Comment 1: It is not clear if there is a standardized protocol for these infants with HA and it sounds like some basic treatments are withheld in some of them due to economic reasons. Thus, this would make it difficult to conclude,

Reply 1: Thank you for your question. We used the standardized protocol in the latest edition of Avery's Diseases of the Newborn and added this (see Page 3, line 18). Most of our cases received the standardized treatment. Some of them couldn't have dialysis due to the technology which we couldn't supply into the critically endangered infants, and some was due to the economic reason.

Comment 2: It would be useful to exclude the premature infants and low birthweights from an analysis because there may be other poor factors associated with the increased morbidity associated with either low birth weight or premature state.

Reply 2: Thanks for this appreciation.

Comment 3: Did all infants get EEG and were any having seizures (either clinical or subclinical) that could lead to a worse outcome?

Reply 3: Thank you for your question. Not all the infants got EEG. Infants with seizures could lead to worse outcome. Two cases in the survival group with seizure left the slow development and the motor defect.

Comment 4: There is no mention of neuroimaging...

Reply 4: There was no standard for evaluation of brain injury due to hyperammonemia, so we could not describe the neuroimaging due to hyperammonemia. We will supply a supplement which contains the neuroimaging description in the infants with MRI.

Comment 5: It is not clear how many days the infants might have had symptoms prior to presentation. Were any of them from families where there was another sibling or they had a prenatal diagnosis?

Reply 5: Thank you for your question. We have added this data about the time between symptoms and presentation (see Page 6, line 18 and table 1). There were some cases with special family history, and we added this data (see Page 6, line 20).

Comment 6: Is it possible to separate factors in the patients with non Urea cycle hyperammonemia? In the organic acidemias, the ammonia is usually lower and it is caused by a different mechanism

Reply 6: Thank you for your suggestion. In this manuscript, we focus on the hyperammonemia in infants. As a result, we couldn't separate the patients with non Urea cycle hyperammonemia.